



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2021-N-0371]

Agency Information Collection Activities; Proposed Collection; Comment Request; Accelerated Approval Disclosures on Direct-to-Consumer Prescription Drug Websites

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA, Agency, or we) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (PRA), Federal Agencies are required to publish notice in the *Federal Register* concerning each proposed collection of information and to allow 60 days for public comment in response to the notice. This notice solicits comments on the proposed study entitled “Accelerated Approval Disclosures on Direct-to-Consumer Prescription Drug Websites.”

**DATES:** Submit either electronic or written comments on the collection of information by **[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**.

**ADDRESSES:** You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before **[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of **[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

### *Electronic Submissions*

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

### *Written/Paper Submissions*

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

*Instructions:* All submissions received must include the Docket No. FDA-2021-N-0371 for "Agency Information Collection Activities; Proposed Collection; Comment Request; Accelerated Approval Disclosures on Direct-to-Consumer Prescription Drug Websites."

Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

*Docket:* For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

**FOR FURTHER INFORMATION CONTACT:** Ila S. Mizrachi, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-7726, [PRAStaff@fda.hhs.gov](mailto:PRAStaff@fda.hhs.gov). The questionnaire is available upon request from [DTCResearch@fda.hhs.gov](mailto:DTCResearch@fda.hhs.gov).

**SUPPLEMENTARY INFORMATION:** Under the PRA (44 U.S.C. 3501-3521), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. “Collection of information” is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the *Federal Register* concerning each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) whether the proposed collection of information is necessary for the proper performance of FDA’s functions, including whether the information will have practical utility; (2) the accuracy of FDA’s estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Accelerated Approval Disclosures on Direct-to-Consumer Prescription Drug Websites

OMB Control Number 0910-NEW

Section 1701(a)(4) of the Public Health Service Act (42 U.S.C. 300u(a)(4)) authorizes the FDA to conduct research relating to health information. Section 1003(d)(2)(C) of the Federal

Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 393(d)(2)(C)) authorizes FDA to conduct research relating to drugs and other FDA regulated products in carrying out the provisions of the FD&C Act.

The Office of Prescription Drug Promotion's (OPDP) mission is to protect the public health by helping to ensure that prescription drug promotion is truthful, balanced, and accurately communicated. OPDP's research program provides scientific evidence to help ensure that our policies related to prescription drug promotion will have the greatest benefit to public health.

Toward that end, we have consistently conducted research to evaluate the aspects of prescription drug promotion that are most central to our mission, focusing in particular on three main topic areas: advertising features, including content and format; target populations; and research quality. Through the evaluation of advertising features, we assess how elements such as graphics, format, and disease and product characteristics impact the communication and understanding of prescription drug risks and benefits. Focusing on target populations allows us to evaluate how understanding of prescription drug risks and benefits may vary as a function of audience, and our focus on research quality aims at maximizing the quality of our research data through analytical methodology development and investigation of sampling and response issues. This study will inform the first topic area, advertising features, including content and format; and the second topic area, target populations.

Because we recognize the strength of data and the confidence in the robust nature of the findings is improved through the results of multiple converging studies, we continue to develop evidence to inform our thinking. We evaluate the results from our studies within the broader context of research and findings from other sources, and this larger body of knowledge collectively informs our policies as well as our research program. Our research is documented on our homepage, which can be found at: <https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-prescription-drug-promotion-opdp-research>. The website includes links to the latest *Federal Register* notices and peer-reviewed publications produced by

our office. The website maintains information on studies we have conducted, dating back to a direct-to-consumer (DTC) survey conducted in 1999.

### *BACKGROUND*

Pursuant to section 506(c) of the FD&C Act (21 U.S.C. 356(c)) and 21 CFR part 314, subpart H (or 21 CFR part 601, subpart E for biological products), FDA may grant accelerated approval to a drug product under section 505(c) of the FD&C Act or a biological product under section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)). This pathway enables faster approval of prescription drugs intended to treat serious or life-threatening illnesses. Accelerated approval may be based on a determination that a drug product has an effect on a surrogate endpoint (for example, a blood test result) that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit (i.e., an intermediate clinical endpoint). In approving a drug under the accelerated approval pathway, the severity, rarity, or prevalence of a condition, and the availability or lack of alternative treatments, are taken into account.

The accelerated approval pathway is limited to certain products intended to treat serious or life-threatening illnesses as there can be “[u]ncertainty about whether clinical benefit will be verified and the possibility of undiscovered risks” (FDA 2014 guidance for industry entitled “Expedited Programs for Serious Conditions--Drugs and Biologics,” available at <https://www.fda.gov/downloads/Drugs/Guidances/UCM358301.pdf>). Sponsors are generally required to conduct post approval studies to verify and describe the predicted clinical benefit, but those confirmatory studies are not complete at the time that the accelerated approval is granted (Ref. 1). In the event that the required post-approval confirmatory studies fail to verify and describe the predicted effect or clinical benefit, a drug’s approval can be withdrawn using expedited procedures.

Under FDA regulations governing physician labeling for prescription drugs, the INDICATIONS AND USAGE section of FDA-approved prescribing information for a drug approved under accelerated approval must include not only the indication (21 CFR 201.57(c)) but also a “succinct description of the limitations of usefulness of the drug and any uncertainty about anticipated clinical benefits...” (21 CFR 201.57(c)(2)(i)(B)). In a guidance, FDA recommended that in addition to these required elements, the INDICATIONS AND USAGE section for drugs approved under accelerated approval should generally acknowledge that continued approval for the drug or indication may be contingent on verification and description of clinical benefit in confirmatory trials (FDA 2019 guidance for industry entitled “Labeling for Human Prescription Drug and Biological Products Approved Under the Accelerated Approval Pathway,” available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM390058.pdf>).

Some DTC websites have included disclosures about accelerated approval, and of those, many included similar content to that seen in the INDICATIONS AND USAGE section of approved labeling. A content analysis of DTC websites for accelerated approval products found that 21 percent of the disclosures used language directly from the approved physician labeling, 79 percent of the disclosures used at least some medical language, but 27 percent of the websites did not include any disclosure that the products attained approval through this pathway (Ref. 2). The same analysis found that 84 percent of accelerated approval disclosures on DTC websites mentioned the approval basis, 68 percent mentioned unknown outcomes, and 47 percent mentioned confirmatory trials (Ref. 2).

OPDP recently conducted a general-population study testing the disclosure of FDA accelerated approval information on a DTC prescription drug website (OMB control number 0910-0872—Experimental Study of an Accelerated Approval Disclosure). The study tested a control condition with no disclosure; a disclosure based on wording used in physician labeling,

including more complex or technical terminology (physician-labeling disclosure); and a consumer-friendly disclosure drafted using simpler language intended to be suited for that audience (consumer-friendly disclosure). The disclosures had three elements: (1) approval basis, (2) unknown outcomes, and (3) confirmatory trials. The physician labeling disclosure was “This indication is based on response rate. An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification of clinical benefit in subsequent trials.” The consumer-friendly disclosure was “In a clinical trial, [Drug X] returned blood counts to normal. However, we currently do not know if [Drug X] helps people live longer or feel better. We continue to study [Drug X] in clinical trials to learn more about [Drug X]’s benefits.” We also varied whether the physician-labeling and consumer-friendly disclosures were presented with low or high prominence (varying the size, color, and location of the disclosure). Preliminary results related to the comprehension of the disclosures tested in that study suggest that the consumer-friendly disclosure helped participants understand information related to the drug’s accelerated approval, but that participants’ understanding was low overall.

#### *NEW PROPOSED STUDY*

The purpose of the current project is to replicate and extend our prior research through two studies by: (1) testing the same experimental conditions with a different study population (cancer survivors and cancer caregivers in study 1) and (2) testing additional consumer-friendly disclosures in study 2. Replication is an important part of science and, if confirmation of prior results is seen, can increase confidence in the results from our first study.

With regard to proposed Study 1, public comments for FDA’s previous accelerated approval disclosure study and other similar FDA studies have suggested conducting studies with people who have been diagnosed with the medical condition or who are caregivers to patients diagnosed with the medical condition that the fictitious drug in the study is intended to treat. Specifically, public comments on the previous study suggested enrolling participants who have



been diagnosed with cancer (i.e., cancer survivors) or people who have cared for loved ones with cancer (i.e., cancer caregivers). Because a number of oncology products are granted accelerated approval, cancer survivors and cancer caregivers are more likely to seek out or be exposed to promotion for accelerated approval products than the general population. They may also be more familiar with cancer-related terms and concepts than the general population. Study 1 will involve cancer survivors and cancer caregivers, a different population than our prior study. It will test the “three element” version of the disclosure as noted above. We will also test the prominence of the disclosure (see table 1).

With regard to study 2, public comments on the original study (Docket No. FDA-2018-N-3138) expressed concern that over-disclosure could dissuade consumers from considering accelerated approval products. One public comment specifically suggested removing the “unknown outcomes” element in the consumer-friendly and physician-labeling disclosures. Based on these comments, in study 2, we propose testing four versions of the consumer-friendly disclosure (table 2): the “three element” version of the consumer-friendly disclosure as well as three other consumer-friendly disclosures that vary with respect to which of these three elements they address. This will allow us to evaluate the impact on participants’ comprehension of the disclosure and perception of the fictitious drug when they view a disclosure with only the approval basis, the approval basis plus information about the unknown outcomes, the approval basis plus information about confirmatory trials, and finally the approval basis plus information about both the unknown outcomes and confirmatory trials. In study 2, the prominence of all the test conditions will be the same and will be the same as the “high prominence” version tested in study 1.

We plan to conduct two pretests not longer than 20 minutes, administered via internet panel, to pilot the main study procedures. We then plan to conduct two main studies not longer than 20 minutes, administered via internet panel. For the pretests and main studies, we will randomly assign the participants to one of the test conditions (see table 1 for the study 1 design

and table 2 for the study 2 design). In both studies, participants will view a website for a fictitious oncology prescription drug. After viewing the website, participants will complete a questionnaire that assesses whether participants noticed the disclosure and their understanding of it, as well as perceptions of the drug's risks and benefits. We will also measure covariates such as demographics and literacy. The questionnaire is available upon request from [DTCresearch@fda.hhs.gov](mailto:DTCresearch@fda.hhs.gov).

For study 1, we hypothesize that participants will be more likely to notice the disclosure when it is presented more, rather than less, prominently. In turn, we expect that participants' perceptions of the drug are more likely to be affected by the disclosure in the high prominence condition. We also hypothesize that participants will be more likely to notice and understand the disclosure and use it to form their perceptions of the drug if they view the consumer-friendly language. For study 2, we hypothesize that participants will be more likely to understand each accelerated approval concept (i.e., confirmatory trials, unknown outcomes) when the disclosure directly addresses the concept, compared with when the disclosure does not directly address the concept. Finally, we will explore whether the inclusion of the concepts of confirmatory trials and unknown outcomes in the disclosure affects participants' perceived risk, perceived risk-benefit tradeoff, perceptions of the website, or information-seeking intentions. To test these hypotheses, we will conduct inferential statistical tests such as logistic regression and analysis of variance.

For the pretests and main studies, we plan to recruit individuals who report a diagnosis with any cancer (except for certain non-melanoma skin cancers) for half the sample and individuals who report being a caregiver for someone with a diagnosis with any cancer (except for certain non-melanoma skin cancers) for the other half of the sample. We will exclude individuals who work for the U.S. Department of Health and Human Services or work in the health care, marketing, advertising, or pharmaceutical industries. With the sample sizes

described below, we will have sufficient power to detect small-sized effects in the main study (table 3).

Table 1.--Study 1 Design

	High prominence	Low prominence	Absent
Physician-labeling version	Condition 1	Condition 3	Condition 5
Consumer-friendly version	Condition 2	Condition 4	

Table 2.--Study 2 Design

	Consumer-friendly disclosure elements			
	Approval basis	Approval basis + unknown outcomes	Approval basis + confirmatory trials	Approval basis + unknown outcomes + confirmatory trials
High prominence	Condition 6	Condition 7	Condition 8	Study 1 Condition 2

FDA estimates the burden of this collection of information as follows:

Table 3.--Estimated Annual Reporting Burden<sup>1</sup>

Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Pretest 1 and 2 screener	3,600	1	1	0.08 (5 minutes)	288
Study 1 and 2 screener	20,600	1	1	0.08 (5 minutes)	1,648
Pretest 1	100	1	1	0.33 (20 minutes)	33
Main Study 1	630	1	1	0.33 (20 minutes)	208
Pretest 2	80	1	1	.33 (20 minutes)	26
Main Study 2	400	1	1	0.33 (20 minutes)	132
Total					2,335

<sup>1</sup>There are no capital costs or operating and maintenance costs associated with this collection of information.

## References

The following references marked with an asterisk (\*) are on display at the Dockets Management Staff (see ADDRESSES), and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at <https://www.regulations.gov>. References without asterisks are not on public display at <https://www.regulations.gov> because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. FDA has verified the website addresses, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

1. Beaver J.A., L.J. Howie LJ, L. Pelosof L, et al. “A 25-Year Experience of U.S. Food and Drug Administration Accelerated Approval of Malignant Hematology and Oncology Drugs and Biologics: A Review.” *JAMA Oncology*. 2018; 4(6):849-856.

doi:10.1001/jamaoncol.2017.5618

2. Sullivan H.W., A.C. O'Donoghue, K.T. David, N.J. Patel. “Disclosing Accelerated Approval on Direct-to-Consumer Prescription Drug Websites.” *Pharmacoepidemiology and Drug Safety*. 2018;27:1277-1280. <https://doi.org/10.1002/pds.4664>

Dated: June 2, 2021.

**Lauren K. Roth,**

*Acting Principal Associate Commissioner for Policy.*

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